**Background and objectives** It has long been recognised that women have a greater prevalence of autoimmune diseases. Rheumatoid arthritis (RA) does not escape this rule with a women:men ratio of 3:1.

X chromosome inactivation (XCI) is a dosage compensation mechanism used by mammals to ensure that XX females and XY males equalise X chromosome gene expression. As a consequence, females are a mosaic of two cell lines, one expressing maternal X-linked and the other expressing paternal X-linked genes with a ratio close to 50:50 when XCI is random.

However skewing, defined as a deviation from the 50:50 ratio has been described in females with autoimmune thyroid diseases, scleroderma and juvenile idiopathic arthritis (for review). The aim of the current study is to test whether women with RA also have a skewed XCI.

**Methods** The highly polymorphic CAG repeat on the first exon of the androgen receptor gene was genotyped, as described elsewhere to determine XCI bias in 84 women with RA and 100 healthy women.

**Results** A total of 54 patients and 69 controls were informative for androgen receptor polymorphism. Among them 31.5% of women with RA (17/54) had a skewed XCI (>80:20) compared to only 17.4% of healthy women (12/69). Only extreme skewing was statistically significant with 18.5% of patients following this pattern and 2.9% of controls (p=0.004).

**Conclusions** Our preliminary data indicate that skewed XCI may be a risk factor for the occurrence of RA in women. Further studies need to be done to analyse whether women who have a skewed pattern have less genetic susceptibilities (shared epitope) or less specific autoantibodies (anti-CCP) as their risk factor is X chromosome linked.

**REFERENCE**

Skewed X chromosome inactivation in rheumatoid arthritis women

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